

Appl. No. 09/592,436  
Amdt. Dated March 3, 2004  
Reply to Office action of December 3, 2003

### **REMARKS/ARGUMENTS**

Reconsideration is respectfully requested of the objection to the claims in view of the Whitehouse et al. reference. In particular, the claims were rejected as being anticipated by Whitehouse et al. Applicant respectfully traverses this rejection.

Claims 1 and 14 have been amended to clearly set forth that the method and apparatus of this invention have a mass selection device before the collision cell to transmit a stream of precursor ions of a selected mass to charge ratio of interest. Therefore the mass-selective specificity of the first fragmentation step is more mass selective since only ions of one  $m/z$  value are injected in the collision cell, and are subsequently fragmented by collision with the gas molecules in the cell.

Whitehouse et al., does not teach nor suggest such a mass selection device before the collision cell. This is because, Whitehouse et al. provides for mass selection within the collision cell. Therefore ions other than the parent or precursor ions may contribute to the fragmentation products and appear in the background spectra.

The Examiner has suggested that Whitehouse et al. discloses applicant's previous amendment at Column 22, lines 1-22. Applicant notes, however, that this section of Whitehouse et al. refers to ion guide 110 (which the Examiner is considering similar to applicant's mass selection device in claims 1 and 14) operating in a wide  $m/z$  range trapping mode.

Accordingly, applicant has further amended claims 1 and 14 to clarify that the mass selection device transmits (to the collision cell) a stream of precursor ions of a selected mass to charge ratio of interest. Applicant submits that Whitehouse et al. does not teach nor suggest the claimed method and apparatus of the present invention, in as much as Whitehouse et al. does not teach a method and apparatus that provides a

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mass selection device that transmits a stream of precursor ions of a selected mass to charge ratio of interest; supplies the stream of precursor ions and a collision gas to a multipole and providing an RF signal to the multipole, whereby the multipole functions as a collision cell; fragments said precursor ions in the RF multipole by collisions with the gas molecules, in order to form primary fragment ions; supplies additional alternating current to the multipole at a frequency selected to cause resonance excitation of a desired primary fragment ion mass-to-charge ratio, whereby ions with said desired primary fragment ion mass-to-charge ratio are excited and undergo collisions with the gas molecules causing production of secondary fragment ions; modulates the alternating current signal applied whereby periods in which said alternating current signal is applied alternate with periods in which the alternating signal is not applied; detects the ion signal after fragmentation with a mass spectrometer and collecting one set of data for one spectrum, representative of the ion spectrum when the alternating current signal is applied and another set of data for another spectrum, representative of the ion spectrum when the alternating current signal is not applied; whereby said other spectrum can be subtracted from said one spectrum, to generate a subtracted spectrum showing the secondary fragment ions without the presence of the primary fragment ions except for any said primary fragment ions which are generated.

Since, in Applicant's submission Whitehouse et al. does not disclose each and every element of the invention as now claimed in claims 1 and 14, there can be no anticipation of those claims (and the dependent claims) as suggested by the Examiner.

Moreover, applicant submits that the Examiner cannot contend that the claimed invention is obvious in view of Whitehouse et al., since it is clear that Whitehouse et al. did not intend for ion guide 110 to operate as a mass selection device to select a stream of precursor ions of a selected mass to charge ratio of interest. In particular, column 21, lines 47-48 of Whitehouse et al., describes the ion guide as operating in a background pressure typically maintained between  $5 \times 10^{-4}$  and  $1 \times 10^{-2}$  torr. This is to be contrasted

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with applicant's invention where Q1 is operated at a low pressure of  $10^{-5}$  torr (see page 10, lines 15-16) needed for an effective mass resolution of a specific m/z value. Again, this is because Whitehouse et al. does not contemplate mass selecting a specific m/z value of interest in ion guide 110 since the Whitehouse et al. invention provides for mass selection within the collision cell.

In applicants submission there is not even the most remote suggestion in any way, shape or form of modifying the Whitehouse et al. method or apparatus for the purposes of the present invention as described and now claimed.

Accordingly, it is respectfully submitted that all of the rejections have been addressed, and that the present application is in condition for allowance and an early notice to that effect is earnestly solicited.

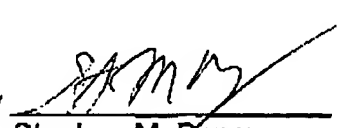
Should the Examiner have any further issues outstanding, applicant invites the Examiner to call the undersigned at (416) 957-1697.

Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

Respectfully submitted,

BERESKIN & PARR

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